

## **Arsenic and Immune Response to Influenza: Implications for Human Health, with Josh Hamilton**

Ernie Hood

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The many adverse health effects caused by chronic arsenic exposure are a concern for the hundreds of millions of people worldwide whose drinking water contains elevated levels of this naturally occurring element. A new rodent study suggests arsenic may also contribute to immune suppression. In this podcast, Josh Hamilton describes the potential implications of this finding for human health, including the possibility that arsenic exposure could help explain why certain populations have been hit harder by pandemic novel H1N1 flu. Hamilton is the senior author of "Low-dose arsenic compromises the immune response to influenza A infection in vivo" and a senior scientist at the Bay Paul Center for Comparative Molecular Biology and Evolution, part of the Marine Biological Laboratory in Woods Hole, Massachusetts.

**AHEARN:** It's *The Researcher's Perspective*. I'm Ashley Ahearn.

Arsenic is a naturally occurring chemical and a known human carcinogen that shows up in groundwater around the world. It's acutely toxic, and now we know that chronic low-dose exposure is linked to many diseases. Arsenic can also affect the way our genes switch on and off—specifically genes that control immune response.

Dr. Josh Hamilton has been studying the relationship between chronic low-dose exposure to arsenic and immune response. He's a senior scientist at the Josephine Bay Paul Center for Comparative Molecular Biology and Evolution at the Marine Biological Laboratory at Woods Hole, Massachusetts.

Dr. Hamilton gave mice drinking water with arsenic in it, then exposed those mice to the H1N1 influenza A virus<sup>1</sup> to study their immune system response. He told science writer Ernie Hood about his findings, which were published in *EHP*.<sup>2</sup>

**HAMILTON:** What we saw was quite interesting, but very unexpected. First, we were able to confirm in the lung that in fact there was immune suppression, not just at the gene level but at the protein and cell level. Certain markers of the innate immune response were in fact suppressed.

The innate immune response is the first line of defense for an infectious agent. Most organisms have this innate immune response. It's a very ancient response to infectious agents. And then higher vertebrates, like us, later in evolution adapted the second line of

defense, the adaptive response, where you develop antibodies to something, and you can respond to it a second time.

This innate immune response was suppressed, and when we then infected them with influenza virus, the animals actually died as a result of what would otherwise be a relatively mild infection. Then, in the animals who did not get arsenic, they went through the normal course of an influenza infection, and then they got better.

**HOOD:** With so many people living in areas of the world with arsenic contamination in well water today, what does the immune compromise that you describe, that you saw in the mouse population, suggest in terms of public health? Are people in these areas more vulnerable to viral or bacterial infection?

**HAMILTON:** Well, that would be our prediction, and in fact there are some epidemiology studies that are coming out now from some parts of the world where there's chronic arsenic exposure where they've shown that babies who are exposed *in utero* through their mothers to arsenic in drinking water in fact have compromised immune systems when they're born, and that leads them to health consequences that are predicted from that immune suppression. And so, as a general phenomenon I think it's probably true that arsenic *is* suppressing the immune response in humans who are exposed. And it would be, I think, pretty reasonable to expect, then, that if they're exposed to influenza or some other infectious agent, that they would not be able to deal with that as effectively.

Typically, people who die of influenza—and worldwide, that's a very large number; 36,000 people a year in the U.S. alone die from influenza every year—many of those you might predict: they're very young, they're very old, they might have other major health problems, particularly lung diseases. But there's always been a group of people who do very poorly or even die from influenza infection for reasons that aren't clear. They seem otherwise healthy. They don't have any known preexisting conditions. And this [arsenic exposure] might be one factor that helps explain some of those problems.

**HOOD:** Are there any public health measures that can be instituted to reduce human exposure to arsenic or potentially to reduce the consequences of exposure to arsenic once it's taken place?

**HAMILTON:** Well, I think the answer to the first question is certainly yes. The simplest thing is to avoid the exposure in the first place. Certainly in the U.S., I would urge

anyone who's on a private well supply to have their water tested. People may not realize that only public water supplies are regulated by the state and federal government, and that private, unregulated wells really are untested unless the homeowner chooses to do that.

As far as the second question, that's really going to require a great deal more research. When somebody's already been exposed to arsenic, it's not clear yet whether simply having them cease exposure will restore them to normal health, or whether more long-term consequences will still occur. There's some epidemiology that suggests that even when the arsenic is gone from our bodies, there's long-term effects that are not very reversible.

**HOOD:** With that in mind, what are the potential long-term implications of your research?

**HAMILTON:** Well, there was an interesting study in Chile that we had an eye on when we did our study in mice.<sup>3</sup> There was a town there that had very high arsenic levels back in the 1960s, and they weren't aware of this arsenic until about 1970. When they realized that that level was high, they switched to an alternative water source. But there was a cohort of people that was exposed to arsenic for about 10 years during the 1960s who've been now followed for health effects for several decades. And even 40 years after cessation of that exposure, the cohort there that was exposed *in utero* and during the first 10 years of life has a 50-fold increased risk of certain lung diseases. And that was really quite unexpected.

**HOOD:** So, how will you plan to pursue this line of research?

**HAMILTON:** Well, one aspect is to engage our epidemiology colleagues in doing more follow-up studies, both on these lung diseases, such as those in Chile, and also looking forward on perhaps whether it influences the course of the flu exposure this coming winter. The other is to go back to the lab and really try and understand the cell and molecular basis for these effects. That might give us clues to how we could either prevent them or ameliorate them once they've occurred.

**AHEARN:** That was Dr. Josh Hamilton talking with science writer Ernie Hood. Dr. Hamilton is a senior scientist at the Josephine Bay Paul Center for Comparative Molecular Biology and Evolution at the Marine Biological Laboratory at Woods Hole, Massachusetts.

And that's *The Researcher's Perspective*. I'm Ashley Ahearn. Thanks for downloading!

## References & Notes

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<sup>1</sup> The study used a different H1N1 subtype from the one responsible for the 2009 H1N1 pandemic.

<sup>2</sup> Kozul CD, et al. Environ Health Perspect 117(9):1441–1447 (2009); doi:10.1289/ehp.0900911.

<sup>3</sup> Smith AH, et al. Environ Health Perspect 114(8):1293–1296 (2006); doi:10.1289/ehp.8832.

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